## REMARKS

Claims 1-62 are pending in the application.

No new matter has been added.

A Notice to Comply With Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures dated December 12, 2001 has been sent by the Patent Office. In the Notice, Applicants were requested to provide a paper copy of the Sequence Listing as well as a copy of the Sequence Listing in Computer Readable Form.

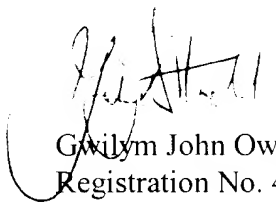
Applicants provide herewith sheets to insert the paper copy of the Sequence Listing. Applicants also provide a copy of the Sequence Listing in Computer Readable Form. Support for the Sequence Listing can be found throughout the application as originally filed. In addition, Applicants provide required statements associated with the submission of paper and computer readable copies of Sequence Listings. Applicants have also amended the specification to insert or correct sequence identifiers.

No new matter has been added.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

Claims 1-62 are in condition for allowance. Applicants respectfully request that this amendment be entered and that claims 1-62 be allowed at this time.

Respectfully submitted,



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Attachments:
Paper copy of Sequence Listing (pages 1-67)
Sequence Listing in Computer Readable Form
Statement in Support of Sequence Listing
Copy of Notice to Comply
Version With Markings To Show Changes Made

## VERSION WITH MARKINGS TO SHOW CHANGES MADE

### In the Sequence Listing

Please insert pages **1-67** containing the Sequence Listing.

### In the Specification

Please amend the specification as follows:

On page 4, please delete the paragraph beginning with "The allatostatins" and insert therefor:

-- The allatostatins are an important group of insect neurohormones controlling diverse functions including the synthesis of juvenile hormones known to play a central role in metamorphosis and reproduction in various insect species. The very first Drosophila allatostatin, Ser-Arg-Pro-Tyr-Ser-Phe-Gly-Leu-NH2 <SEQ ID NO:161> (i.e., drostatin-3), was isolated from Drosophila head extracts (Birgulet al., The EMBO J., 1999, 18, 5892-5900). Recently, a Drosophila allatostatin preprophormone gene has been cloned which encodes four Drosophila allatostatins: Val-Glu-Arg-Tyr-Ala-Phe-Gly-Leu-NH2 <SEQ ID NO:164> (drostatin-1), Leu-Pro-Val-Tyr-Asn-Phe-Gly-Leu-NH2 <SEQ ID NO:165> (drostatin-2), Ser-Arg-Pro-Tyr-Ser-Phe-Gly-Leu-NH2 <SEQ ID NO:161> (drostatin-3) and Thr-Thr-Arg-Pro-Gln-Pro-Phe-Asn-Phe-Gly-Leu-NH2 <SEQ ID NO:166> (drostatin-4) (Lenz et al., Biochem. Biophys. Res. Comm. 2000, 273, 1126-1131). The first Drosophila allatostatin receptor was cloned by Birgul et al. and shown to be functionally activated by drostatin-3 via Gi/Go pathways (Birgul et al., EMBO J. 1999, 18, 5892-5900). A second putative Drosophila allatostatin receptor (i.e., DARII). has been recently cloned (Lenz et al., Biochem. Biophys. Res. Comm. 2000, 273, 571-577). The DARII receptor cDNA (accession No. AF253526) codes for a protein that is strongly related to the first Drosophila allatostatin receptor. However, to date no functional activation of DARII by allatostatins has been reported. --

On page 4, please delete the paragraph beginning with "The sulfakinins" and insert therefor:

-- The sulfakinins are a family of insect Tyr-sulfated neuropeptides. They show sequence and functional (myotropic effects, stimulation of digestive enzyme release) similarity to the vertebrate peptides gastrin and cholecystokinin. A gene encoding two sulfakinins (also called drosulfakinins), DSKI [Phe-Asp-Asp-Tyr(SO3H)-Gly-His-Met-Arg-Phe-amide] [<SEQ ID NO: 160>] <SEQ ID NO:155> and DSKII [Gly-Gly-Asp-Asp-Gln-Phe-Asp-Asp-Tyr(SO3H)-Gly-His-Met-Arg-Phe-amide] [<SEQ ID NO: 161>] <SEQ ID NO:160>, has been identified in Drosophila melanogaster (Nichols, (Mol. Cell Neuroscience, 1992, 3, 342-347; Nichols et al., J. Biol. Chem. 1988, 263, 12167-12170). The C-terminal heptapeptide sequence, Asp-Tyr(SO3H)-Gly-His-Met-Arg-Phe-amide <SEQ ID NO: 162>, is identical in all sulfakinin identified so far from insects that are widely separated in evolutionary terms. The conservation of the heptapeptide sequence, including the presence of the sulfated Tyr residue, in widely divergent insect taxa presumably reflects functional significance of this myotropic "active core" (Nachman & Holman, in Insect Neuropeptides; chemistry, biology and action, Menn, Kelly & Massler, Eds., 1991, pp. 194-214, American Chemical Society, Washington, D.C.). To our knowledge, to date no receptors for insect sulfakinins have been identified. --

On page 42, please delete the paragraph beginning with "The modulators" and insert therefor:

-- The modulators of the invention exhibit a variety of chemical structures, which can be generally grouped into non-peptide mimetics of natural GPCR receptor ligands, peptide and non-peptide allosteric effectors of GPCR receptors, and peptides that may function as activators or inhibitors (competitive, uncompetitive and non-competitive) (*e.g.*, antibody products) of GPCR receptors. The invention does not restrict the sources for suitable modulators, which may be obtained from natural sources such as plant, animal or mineral extracts, or non-natural sources such as small molecule libraries, including the products of

combinatorial chemical approaches to library construction, and peptide libraries. Examples of peptide modulators of GPCR receptors exhibit the following primary structures: GLGPRPLRFamide <SEQ ID NO: 49> , GNSFLRFamide <SEQ ID NO: 168> , GGPQGPLRFamide <SEQ ID NO: 102> , GPSGPLRFamide <SEQ ID NO: 103> , PDVDHVFLRFamide <SEQ ID NO: 150> , and pyro-EDVDHVFLRFamide <SEQ ID NO: 167>. --

On page 95, please delete the paragraph beginning with "Aliquots (5-10 µl containing 1-5 µg protein) of cytosol" and insert therefor:

-- Aliquots (5-10 µl containing 1-5 µg protein) of cytosol are mixed with 1 mM MAPK Substrate Peptide (APRTPGGRR [(SEQ ID NO: )] <SEQ ID NO: 163> , Upstate Biotechnology, Inc., N.Y.) and 50 µM [$\gamma$-$^{32}$P]ATP (NEN, 3000 Ci/mmol), diluted to a final specific activity of ~2000 cpm/pmol, in a total volume of 25 µl. The samples are incubated for 5 minutes at 30°C, and reactions are stopped by spotting 20 µl on 2 $cm^2$ squares of Whatman P81 phosphocellulose paper. The filter squares are washed in 4 changes of 1% $H_3PO_4$, and the squares are subjected to liquid scintillation spectroscopy to quantitate bound label. Equivalent cytosolic extracts are incubated without MAPK substrate peptide, and the bound label from these samples are subtracted from the matched samples with the substrate peptide. The cytosolic extract from each well is used as a separate point. Protein concentrations are determined by a dye binding protein assay (Bio-Rad Laboratories). Agonist activation of the receptor is expected to result in up to a five-fold increase in MAPK enzyme activity. This increase is blocked by antagonists. --